Formula TWO: Mechanism of Action [Multiple Mode of Action] Claims:

1. Decrease cravings, Eat for FUEL
   • Act on the gut-brain axis by regulating the mediators of appetite
   • Regulates serum levels of the appetite hormone ghrelin
   • Maintains the release of satiety hormone, leptin, from adipocyte
   • Reduction in the secretion of neuropeptide and appetite neuromediator Y (NPY)

2. Works at the adipocyte (fat storage) level
   • Mimics the phenotype change from white to beige that occurs in adipose cells
   • Stored energy to metabolism-driven cells
   • Prevents further storage of fat within adipose tissue

3. Increases resting energy expenditure [energy used by the body]
   • Enhances physiological lipolysis, boosting the release of Free Fatty Acids (FFAs)
   • Inhibition of PDE-3, leading to higher levels of cAMP
   • Increases the breakdown of triglycerides and release of FFAs

4. Burns Fat, continue to lose fat [100% weight loss from fat mass]
   • Intensifies FFA metabolism through UCPs expression promotion
   • Increases cAMP [Cyclic adenosine monosphate]
   • Promotes higher expression of uncoupling proteins in beige adipose tissue
   • Releases FFA instead of restored as adipocytes (fat)

Efficacy Claims:

• 100% weight loss from fat mass

• Abdominal fat and waist circumference decrease significantly [6% reduction in fat mass ratio, 5cm waist circumference reduction (2 inches)]

• Rebalanced body composition to have more muscle mass and less fat mass.

• Daily caloric intake drops by 600kcal

• Reduced appetite for sweet foods

- Increases metabolic rate [energy burned at rest]
- 65% of total fat loss is from the trunk area
- Continue to lose weight and reduce body fat mass after 20 weeks of supplementation

Clinical/Mechanistic Studies:

1. Jung EY, Lee JW, Hong YH, Chang UJ, Suh HJ. Low Dose Yeast Hydrolysate in Treatment of Obesity and Weight Loss. *Prev Nutr Food Sci*. 2017;22(1):45-49. doi:10.3746/pnf.2017.22.1.45
2. Jung EY, Cho MK, Hong YH, et al. Yeast hydrolysate can reduce body weight and abdominal fat accumulation in obese adults. *Nutrition*. 2014;30(1):25-32. doi:10.1016/j.nut.2013.02.009
3. Jung EY, Lee JW, Hong YH, Chang UJ, Suh HJ. Low Dose Yeast Hydrolysate in Treatment of Obesity and Weight Loss. *Prev Nutr Food Sci*. 2017;22(1):45-49. doi:10.3746/pnf.2017.22.1.45
4. Park Y, Kim JH, Lee HS, et al. Thermal stability of yeast hydrolysate as a novel anti-obesity material. *Food Chem*. 2013;136(2):316-321. doi:10.1016/j.foodchem.2012.08.047
5. Jung EY, Hong YH, Kim JH, et al. Effects of yeast hydrolysate on hepatic lipid metabolism in high-fat-diet-induced obese mice: yeast hydrolysate suppresses body fat accumulation by attenuating fatty acid synthesis. *Ann Nutr Metab*. 2012;61(2):89-94. doi:10.1159/000338441
6. https://www.researchgate.net/publication/316073223_Low_Dose_Yeast_Hydrolysate_in_Treatment_of_Obesity_and_Weight_Loss
7. Dallas C, Gerbi A, Tenca G, Juchaux F, Bernard FX. Lipolytic effect of a polyphenolic citrus dry extract of red orange, grapefruit, orange (SINETROL) in human body fat adipocytes. Mechanism of action by inhibition of cAMP-phosphodiesterase (PDE). *Phytomedicine*. 2008;15(10):783-792. doi:10.1016/j.phymed.2008.05.006
8. Dallas C, Gerbi A, Elbez Y, Caillard P, Zamaria N, Cloarec M. Clinical study to assess the efficacy and safety of a citrus polyphenolic extract of red orange, grapefruit, and orange (Sinetrol-XPur) on weight management and metabolic

parameters in healthy overweight individuals. *Phytother Res*. 2014;28(2):212-218. doi:10.1002/ptr.4981

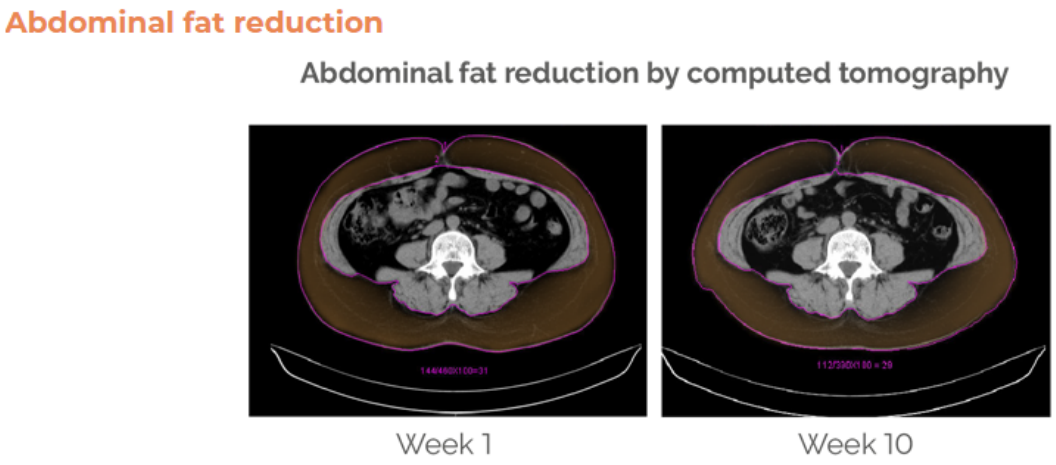
9. Cases J, Romain C, Dallas C, Gerbi A, Rouanet JM. A 12-week randomized double-blind parallel pilot trial of Sinetrol XPur on body weight, abdominal fat, waist circumference, and muscle metabolism in overweight men. *Int J Food Sci Nutr*. 2015;66(4):471-477. doi:10.3109/09637486.2015.1042847
10. Berry SE, Valdes AM, Drew DA, et al. Human postprandial responses to food and potential for precision nutrition [published correction appears in Nat Med. 2020 Nov;26(11):1802]. *Nat Med*. 2020;26(6):964-973. doi:10.1038/s41591-020-0934-0
11. Kim MS, Yang HJ, Kim SH, Lee HW, Lee MS. Effects of Kimchi on human health: A protocol of systematic review of controlled clinical trials. Medicine (Baltimore). 2018;97(13):e0163. doi:10.1097/MD.0000000000010163
12. Correction: Nutrikinetics and urinary excretion of phenolic compounds after a 16-week supplementation with a flavanone-rich ingredient - Food & Function (RSC Publishing)

Appendix:

POPULATIONS	**54 subjects** Men and women BMI> 25 kg/m^2 Age: 20-50 years old	**30 subjects** Women BMI> 25 kg/m^2 Age: 20-60 years old
PROTOCOLS	**Abdominal fat distribution** Computed tomography No specific exercise and diet patterns Food record (*Can-Pro*)	**Body composition** Impedance bioelectrical scale No specific exercise and diet patterns Food record (*Can-Pro*)
INTAKES	**SACHETS** 2 x 500 mg/day	**CAPSULES** 2 x 250 mg/day

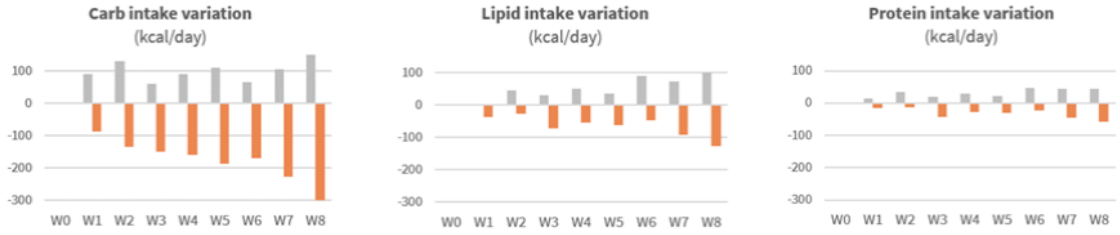
YEAR & DURATION	**2017** **20 weeks (16+4)**	**2019** **12 weeks**
POPULATIONS	**77 subjects** Caucasian population BMI: 25-40 kg/m^2 Age: 29-52 years old	**86 subjects** Asian population BMI: 24-30 kg/m^2 Age: 25-62 years old
PROTOCOLS	**Body composition** DXA scan Recommended individualised **normo-caloric diet** *(Harris and Benedict)*	**Body composition** DXA scan Recommended **hypo-caloric diet** *(-500 kcal hypocaloric diet)*
INTAKES	**CAPSULES** 2 x 450 mg/day	**TABLETS** 1 x 900 mg/day

A.



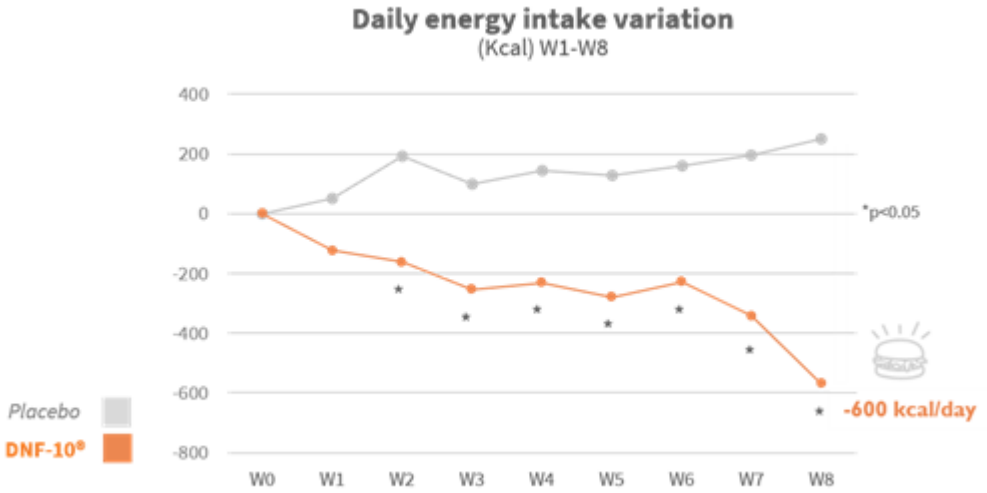
100% weight loss from fat mass, leading to a 6% reduction in the fat mass ratio.

B.

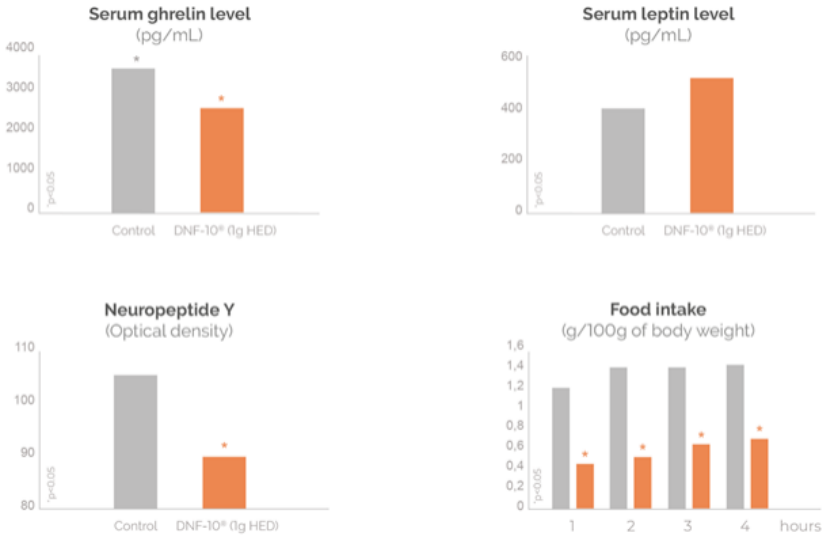


After 2 months, daily caloric intake drops by 600kcal.

Reduction of appetite for sweet foods.



C.



Lowers ghrelin secretion.

Lowers expression of NPY in the hypothalamus.